In June, the agency published draft guidance for the broader pharmaceutical industry reflecting the modernized eligibility criteria recommendations. More inclusive trial designs were also suggested, such as the use of so-called expansion cohorts, which could involve lower-dose interventions for older patients. And the agency encouraged the drug industry to make trial participation less burdensome, for example, by offering travel expenses or by replacing some site visits with electronic communication.

But the FDA lacks the teeth to enforce its guidance. Legally granting the agency increased authority to incentivize and make trial participation less burdensome, for example, by offering travel expenses or by replacing some site visits with electronic communication.

The science behind food’s effects on human health is discovering some tasty benefits.

Berries and Grapes Linked With Memory Boost
As the world’s elderly population races toward an estimated 2 billion by 2050, memory loss is expected to take a substantial toll. But recent research shows that polyphenols from grapes and blueberries combined may help boost declining memory among some older adults.

The study by investigators in France and Canada built not only on their own work in mice, but also on other preclinical and clinical studies showing that blueberries and grapes or their extracts may offer benefits for age-related cognitive decline. Their previous animal research also showed a synergistic effect—grape extract enhanced the absorption of polyphenols in the blueberry extract.

To determine whether an extract of both fruits may affect human cognition, the investigators enrolled 215 men and women aged 60 to 70 years in a 6-month clinical trial. They randomized the participants to receive a placebo or 600 mg per day of a polyphenol-rich grape and blueberry extract that contained 258 mg of flavonoids.

At the trial’s start, the investigators administered several cognitive ability tests. The primary outcome was results from visuospatial skills and episodic memory tests in which participants watched boxes, some that contained patterns, open on a touchscreen computer. When the patterns then appeared in the middle of the screen, participants had to match them to the appropriate box. Additional testing assessed episodic verbal memory and working memory.

Although all participants improved on the touchscreen computer test after 6 months, the investigators reported no difference in performance between the extract and placebo groups. But when they divided the participants into 4 groups according to their baseline test performance, the investigators found significant improvement among extract recipients with the greatest cognitive decline. In this group, cognitive age estimated from baseline test results improved by nearly 14 years compared with about 5½ years in the placebo group. Overall, the extract group also improved in verbal recall.

"[O]ur study confirms the need to define a recommended dietary allowance for flavonoids and revisit recommendations for foods rich in these bioactives," the authors concluded.

Why Cilantro May Curb Seizures
Cilantro is an herb of many faces. It’s a staple in salsa and perfect for pickling. Not only were its seeds found in King Tut’s tomb, but...
it has a folk medicine history as an anticonvulsant. Now recent research explains why it’s been used to combat some seizures.

In a recent FASEB Journal study, researchers at the University of California, Irvine (UCI), reported that cilantro, or Coriandrum sativum, is a potent activator of neuronal voltage-gated potassium channel subfamily Q (KCNQ). Mutations in most of the genes that express this family of potassium channels can lead to heart disease, deafness, and severe epilepsy syndromes that are resistant to modern anticonvulsants.

By screening cilantro leaf metabolites, the researchers found that one—the long-chain fatty aldehyde (E)-2-dodecenal—activates several KCNQ channels, including the predominant neuronal and cardiac isoforms that regulate electrical activity in the brain and heart. “Dodecenal binds to a specific part of the potassium channels to open them, reducing cellular excitability” and seizure activity, Geoff Abbott, PhD, professor of physiology and biophysics at the UCI School of Medicine, said in a statement. The metabolite also delayed some chemically induced seizures in mice.

Abbott said the finding “is important, as it may lead to more effective use of cilantro as an anticonvulsant or to modifications of dodecenal to develop safer and more effective anticonvulsant drugs.”

Do Mushrooms Really Protect Against Cardiometabolic Disease?

Mushrooms may be rich in vitamins, minerals, and bioactive compounds such as polysaccharides, but recent research indicates that the fungi may not measure up to claims that they protect against cardiovascular disease and type 2 diabetes.

Investigators from Harvard Medical School and Harvard’s T.H. Chan School of Public Health noted that evidence from human studies to support mushrooms’ cardiometabolic benefits is limited. So they turned to 2 large, prospective, long-running cohort studies—the Nurses’ Health Study and the Health Professionals Follow-up Study—to examine whether eating mushrooms may reduce cardiometabolic disease risks or affect related biomarkers such as low-density lipoprotein (LDL) cholesterol.

Their analysis involved 67 139 women, 43 541 men, and more than 2 million person-years of follow-up. Based on food-frequency questionnaires, the investigators separated participants into categories according to how often they ate mushrooms. The cardiometabolic disease biomarkers they evaluated in addition to LDL cholesterol included total and high-density lipoprotein cholesterol, triglycerides, C-reactive protein, and C peptide.

Among participants who ate 5 or more servings of mushrooms per week, the investigators found no difference in risk of cardiovascular disease or type 2 diabetes compared with those who ate mushrooms less than once a month. They also found no association between mushroom consumption and disease biomarkers.

The investigators did, however, note limitations: Mushroom consumption in their study was low; about half the participants ate them less than once a week. In addition, they assessed mushroom consumption only once, at baseline. “Given the wide popularity of mushrooms and the growing interest in their potential clinical effects, more prospective cohort studies addressing the limitations of this study are warranted,” the researchers wrote.

Note: Source references are available through embedded hyperlinks in the article text online.

The JAMA Forum

Heritable Genome Editing—Edited Eggs and Sperm to the Rescue?

Eli Adashi, MD, MS; I. Glenn Cohen, JD

“[W]e might anticipate the in vitro culture of germ cells... coupled with recognition, selection and integration of the desired genes...” Nobel Laureate Joshua Lederberg, PhD (1963)

Heritable genome editing is widely predicted to render inborn afflictions a thing of the past. Topping the list of edit-worthy maladies are single-gene disorders for which preimplantation genetic diagnosis is unworkable. In addition, an insufficient number of viable embryos without the disease mutation is an important limitation in preimplantation genetic diagnosis, and in such cases, heritable genome editing might offer an alternative strategy.

Constraints along these lines have frequently undermined some families’ attempts to have a baby—a “savior sibling”—who could serve as a stem cell donor to a sick older sibling who might benefit. Heritable genome editing could also be brought to bear on disease-predisposing gene variants, such as a variant of the APoE gene that contributes to Alzheimer disease risk; a variant of the LPA gene that contributes to atherosclerotic cardiovascular disease; a variant of the MYPBC3 gene that causes hypertrophic cardiomyopathy; and variants in BRCA genes that increase breast and ovarian cancer risk. Currently, the focus of preclinical research, with safety and efficacy in mind, heritable genome editing remains years away from the clinic.

Preclinical research efforts to replace mutant alleles with wild-type counterparts have thus far been limited to human embryos. Such efforts have formidable technical challenges, including introduction of unintended genomic insertions, deletions, and rearrangements, which cannot be tolerated in the clinical context. Nothing less than unyielding editing precision is required to preclude cross-generational harm. An additional challenge to editing the human embryo is the uniformity imperative—ensuring that all the embryo’s cells are appropriately edited. Failure to edit the entire cellular complement of the embryo to exclude mosaicism (in this case, a mixture of edited and unedited cells) is clinically inviable. One final challenge of note is the required validation of edited embryos as transfer eligible. Impeccable editing fidelity as well as uniformity must be demonstrated prior to embryo transfer. At present, however, such reliable assessment is technologically infeasible, and accomplishing this goal may require new technologies.